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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/018,194	02/04/1998	BARBARA A. GILCHRIST	BU94-15A2	9447

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/018,194	GILCHREST ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-36 and 45-73* is/are pending in the application.

4a) Of the above claim(s) *45-52,54 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-36,53,56 and 57* is/are rejected.

7)☒ Claim(s) *58-73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment filed 10 May 2004 has been entered. Claims 56-73 have been added and read on the elected invention. Claims 1-32 have been cancelled. Claims 45-52, 54 and 55 were previously withdrawn by the examiner (29 January 2004). Claims 33-36, 53 and 56-73 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and/or Rejections

35 U.S.C. § 112, first paragraph, Enablement.

Claims 33-36 and 53 are rejected under 35 USC 112, first paragraph because the subject matter was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reasons for this rejection were set forth at pages 3-6 of the previous office action (29 January 2004). Briefly, the specification is not enabling for the limitations of the claims wherein inhibition of apoptosis in epidermal keratinocytes is used as a method of maintaining hair growth. As discussed in the previous Office Action (29 January 2004) maintenance of hair growth in the skin of mammals involves a variety of interacting factors, including immunological conditions and the influences of reproductive

hormones, as well as many unknown factors (Straile, et al, 1961, J. Exp. Zool. 148: 205-221). There are also different mechanisms of hair maintenance and loss depending on the area of skin studied.

Claims 33-36 and 53 read on a method of maintaining hair growth in a vertebrate by inhibiting apoptosis in keratinocytes. The claimed ligands to be used for the method of the invention are the "KGA" peptides of SEQ ID NO: 4, 9 and 10, as well as antibodies. Mild UV radiation was used to cause apoptosis in mouse follicles. It is this apoptosis that is inhibited by the NGF-derived "KGA" peptides. Applicants have further shown that the peptide ligands extend the active stages of the hair life cycle, leading to what are essentially "younger" and longer-lasting hair shafts in these experiments (for reviews see: Paus, et al, 1997, J. Invest. Dermatol. 2(1): 61-68; Detmar, et al, 1993, J. Invest. Dermatol., 101: 130S-134S).

Applicants explain further in the Response of 26 April 2004:

"UV irradiation of keratinocytes in cell culture is not meant to mimic, and does not mimic, the factors that contribute to male pattern baldness or to alopecia areata. Rather, UV is used only as an initiating event for apoptosis. In the model of hair loss using UV on cells in culture, the radiation is brief -- only long enough to activate pathways for the cells to commit suicide. The p75 pathway is a common final pathway to cause apoptosis, found in all cells. UV is not the relevant stimulus that causes male pattern baldness, but sets in motion pathways going through the p75 receptor. The p75 receptor governs transitions of anagen through telogen. Applicants' method blocks the transition to catagen" (pages 2-3).

Despite Applicants' arguments, there is no enabling discussion or working examples disclosed in the instant application that definitively demonstrate that p75 is the

final target for apoptotic processes in all hair follicles under all conditions. In other words, the particularly intractable hair-loss conditions such as male-pattern baldness and Alopecia areata --treatments for which are encompassed by Claims 33-36 and 53-- may have underlying mechanisms of apoptosis that are unrelated to p75 and would not be treatable by the claimed methods. Applicants' have failed to demonstrate that p75 is the final common pathway in all hair-loss related conditions, as encompassed by Claims 33-36 and 53, and that their methods of treating hair loss would therefore operate as intended under all conditions. The specification *does* describe correlations between bcl-2 levels and NGF concentrations bathing the cells. This implies one mechanism for apoptotic cell death caused by the UV irradiation that involves this tumor-suppressor gene. However, the nexus between bcl-2 levels and p75 has not been established, and indeed may imply that different apoptotic mechanisms can cause hair loss in different cells or under different conditions.

Furthermore, Applicants are not enabled for use of an antibody used as a ligand that would inhibit apoptosis, as recited in Claim 53. The state of the art is such that antibodies that *bind* with high affinity can be made to almost any peptide. However, to produce an antibody that has the precise configuration to bind to an active site on a receptor is a rare event. Such an antibody in this case, for example, might have to comprise the KGA peptide located in the correct location on its F(ab) fragment, an extremely unlikely event.

Applicants are also not enabled for use of a "pseudo-ligand" that does not include the KGA fragment of NGF, as recited in Claims 33, 53, 56, 62 and 68. Although "pseudo-ligand" is defined in the Specification (page 21, for example), it is an

unconventional usage and leads to the inclusion of a variety of ligands that the Applicant has not enabled for use in the claimed methods. Applicants may define "pseudo-ligand" in the claims, or remove the term.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation required to determine how to use the disclosed polypeptides to maintain hair growth in mammalian skin under all conditions of hair loss, the lack of direction or guidance in the specification regarding the same, the lack of working examples that measure hair growth in a vertebrate, the state of the art which acknowledges the complexity of inducing new hair growth in mammalian skin, and the breadth of the claims which embrace methods of maintaining hair growth that "override" other apoptotic mechanisms --undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

35 USC § 112, first paragraph – Written Description.

Claims 56, 62 and 68 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 56, 62 and 68 are directed to methods of using a *pseudo-ligand* to inhibit apoptosis in keratinocytes.

The specification teaches use of the "KGA" peptides derived from NGF. However, the specification does not teach functional or structural characteristics of all

ligands or *pseudo-ligands* used for the claimed methods. The description of one genus of NGF-derived polypeptides is not adequate written description of other genera of functionally equivalent polypeptides or non-polypeptides that may bind p75.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the KGA peptides referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed *pseudo-ligands*, and therefore, would not know how to use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the KGA peptides described in the instant Specification, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112,

first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

Claims 33-36, 53, 56 and 57 are rejected. Claims 58-73 are objected to for depending from rejected base claims, but would be allowable if written in independent form.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

SLW

4 August 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER